0022-5282/81/2109-0753$02.00/0
THE JOURNAL OF TRAUMA

Vol. 21, No. 9
Printed in U.S.A.

Burn Wound Infection

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Ninety-seven of 763 patients admitted to a burn center during a 3-year period had histologically confirmed bacterial or fungal burn wound invasion. Nine of these 97 patients survived and 88 died. Burn wound infection was the principal cause of death in 57 patients and was diagnosed perimortem in an additional 31 patients but was not judged to be the primary cause of death. *Pseudomonas aeruginosa* continues as the most frequent offending organism. The variety of mycotic and bacterial organisms identified, however, suggests that the compromise of the host is the critical factor, and not any particular microorganism. A variety of combinations of treatments are described: the selection of treatment depends upon the type and extent of infection.

In recent years, burn wound infections caused by microorganisms other than *Pseudomonas aeruginosa* have become more prominent. The histologic characteristics of such infections differ from those of invasive burn wound sepsis as originally described (7–10). In 1961, Rabin identified the burn wound as a portal for bacterial entry into the blood (7). Subsequently, Teplitz (8–10) defined the pathogenesis of *Pseudomonas* invasive burn wound sepsis (BWS) and these studies led to the development of effective topical chemotherapy which has controlled *Pseudomonas* burn wound infection in most patients (2, 4). Pruitt (5) described the use of burn wound biopsy for histologic and microbiologic monitoring of the burn wound and as a guide for timely and specific treatment of burn wound infection.

The following report reflects the current spectrum of burn wound infections and their treatment at the U.S. Army Institute of Surgical Research.

MATERIALS AND METHODS

We reviewed the records of 763 patients consecutively admitted to the U.S. Army Institute of Surgical Research from 1 January 1976 through 31 December 1978 and selected the records of 97 patients with histologically confirmed bacterial or fungal burn wound invasion as the basis for this report.

Histologic burn wound invasion was classified as a primary cause of death when such invasion was the first or predominant complication in the patient's postburn course. Incidental burn wound invasion was defined as histologically documented invasion occurring after other established complications had caused hypotension and decreased peripheral perfusion. Burn wound sepsis is defined as microbial invasion of viable tissue, either subjacent or adjacent to the burn wound, producing the clinical findings associated with septicemia. Burn wound invasion may be focal or generalized. Clinically, the likelihood of septicemia appears to increase as the area of wound invasion increases and is relatively infrequent in patients with focal invasion or even multifocal invasion when the area of infection is less than 20% of the total body surface. Generalized burn wound invasion is considered to be present when the infection involves an area exceeding 20% of the total body surface (TBS) and is associated with a higher frequency of septicemia.

RESULTS

Seven hundred sixty-three patients with an average TBS burn of 35% were treated during the period of this review and 218 patients died; this number of deaths is consistent with the mortality predicted on the basis of burn size and age of the study population.

Ninety-seven of the 763 patients had histologically confirmed bacterial or fungal burn wound invasion. The average extent of burn in these 97 patients was 56% TBS, with an average 26% full-thickness component. The average age of these patients was 30.4 years; age ranged from 2 to 81 years. Seventy-one patients were males and 26 females, reflecting the predominance of male patients admitted to this center.

Eighty-eight of these 97 patients died with a pre- or postmortem histologic diagnosis of burn wound invasion.

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Presented at the Fortieth Annual Session of the American Association for the Surgery of Trauma, Phoenix, Arizona, 18 September 1980.

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In 31 (35%) of these 88 patients who had burns involving an average of 61% TBS and an average age of 32 years, the diagnosis of burn wound invasion was considered an incidental finding and was not considered to have been the cause of death (Table I). In this group of 31 patients, pneumonia was the primary septic process in 27 (20 of these 27, or 74%, had antecedent inhalation injury), while suppurative thrombophlebitis, infectious hepatitis, acute myocardial infarction, and pulmonary embolus were considered the primary cause of death in one additional patient each. Burn wound invasion was identified only after septic or cardiogenic shock had been present in these 31 patients. Twelve (39%) had focal burn wound invasion and four of the 12 patients had positive blood cultures. The remaining 19 (61%) had generalized burn wound invasion and 14 had positive blood cultures (Table II).

In 57 of the 88 patients (65%), in whom burn wound invasion was the principal cause of death, the average extent of burn was 60% of the total body surface and the average age was 31 years. The distribution of organisms recovered by burn wound biopsy is shown in Table III. Fifty-four (95%) of these patients had generalized burn wound invasion and 50 (93%) had blood cultures positive for the organisms recovered from the wound (Table II).

Seventy-five of the 97 patients had burn wound invasion by bacteria alone or in combination with a mycotic organism. The bacterial genera recovered by burn wound biopsy in addition to *Pseudomonas* included *Citrobacter*, *Enterobacter*, *Klebsiella*, and *Staphylococcus*; the mycotic organisms included *Alternaria*, *Aspergillus*, *Candida*, *Coccidiodes*, *Phycomyces*, and *Rhizopus*. In 69 of these 75 patients (92%), the causative organism was recovered by blood culture. However, in 22 of the 97 patients, the wound was invaded with mycotic organisms and in only five were blood cultures positive for the causative organisms.

Nine of 97 patients (9%) with histologic burn wound invasion survived. The average age of the surviving patients was 21 years and the average burn size was 51% TBS, ranging from 32% TBS to 71% TBS with a 17% average extent of full-thickness injury. Four of nine surviving patients had *Pseudomonas aeruginosa* wound infection, one had *Klebsiella* infection, two had fungal infection, and two had combined fungal and bacterial infection. Six of nine surviving patients (66%) had focal burn wound invasion and four of these six had the same microorganism isolated by blood culture. Only three of nine surviving patients had generalized burn wound invasion, of whom two had positive blood cultures. Of the five surviving patients with bacterial burn wound invasion, two had generalized burn wound invasion while three had focal burn wound invasion. One patient with *Aspergillus* invasion had generalized wound infection

TABLE I
97 patients with confirmed burn wound invasion (BWI)

	Survivors	BWI as Incidental Finding	BWI as Cause of Death
Number of patients	9 (9%)	31 (35%)	57 (65%)
Average age	21 Years	32 Years	31 Years
Range	12–31 Years	2–73 Years	2–81 Years
Average total extent of burn	51%	61%	60%
Average extent of full-thickness burn	17%	32%	23%
Inhalation injury present	3 (33%)	22 (77%)	16 (28%)

TABLE III
Microorganisms causing burn wound invasion

	Survivors	BWI—Incidental	BWI—Cause of Death	Totals
Pseudomonas	4	8	32	44
Other Gram-negative bacteria	1	3	12	16
Staphylococcus	0	1	0	1
Mixed bacterial	0	2	6	8
Bacterial/mycotic	2	4	4	10
Mycotic	2	13	3	18
Totals	9	31	57	97

TABLE II
Extent and type of burn wound invasion (BWI)

	Survivors (9 Patients)		BWI—Incidental Finding (31 Patients)		BWI as Cause of Death (57 Patients)		Totals	
	Biopsy	Positive Blood Culture	Biopsy	Positive Blood Culture	Biopsy	Positive Blood Culture	Biopsy	Positive Blood Culture
Focal bacterial	3	3	5	3	2	2	10	8
Generalized bacterial	2	2	9	7	44	43	55	52
Focal mycotic	1	0	7	0	0	0	8	0
Generalized mycotic	1	0	6	2	7	3	14	5
Focal bacterial/mycotic	2	1	0	0	0	0	2	1
Generalized bacterial/mycotic	0	0	4	4	4	4	8	8
Totals	9	6	31	16	57	52	97	74

while the three patients with either fungal or combined fungal and bacterial infection had focal infection.

Treatment of the five surviving patients with bacterial burn wound invasion (four *Pseudomonas* and one *Klebsiella*) included intravenous administration of antibiotics to which the invading organisms were sensitive and subeschar infiltration of a semisynthetic penicillin (3). Excision of the infected burn wound was carried out in four of these five surviving patients; the two surviving patients with histologically documented fungal burn wound invasion were treated with systemic antifungal agents followed by excision of the burn wound. The two surviving patients with histologic and microbiologic evidence of combined bacterial and fungal burn wound invasion were treated preoperatively with systemic antimicrobial agents followed by excision of the infected burn wound.

DISCUSSION

The terms burn wound sepsis and burn wound invasion, although commonly used interchangeably, are not synonymous since burn wound sepsis describes the clinical syndrome of septicemia in association with histologic evidence of microbial invasion extending from burn into viable tissue. Burn wound invasion, however, is considered to be present even in the absence of septicemia when extension of microorganisms into viable tissue subjacent or adjacent to the burn wound is identified by histologic means. A quantitative count of microorganisms from a burn wound biopsy which exceeds 1×10^5 organisms per gram of tissue is suggestive of burn wound infection but unless microorganisms are histologically identified in viable tissue, a diagnosis of burn wound invasion cannot be confirmed.

Burn wound invasion may be focal, multifocal, or generalized. Clinically, the likelihood of septicemia appears to increase as the area of burn wound invasion increases. Septicemia caused by the burn wound infection is less frequent in patients with focal invasion (52% in this series) and even in patients with multifocal invasion when the areas of infection involve less than 20% of the total body surface. Generalized burn wound invasion is considered to be present when the infection involves an area greater than 20% of the body surface area and is associated with a high frequency of septicemia (91% in this series).

Since 1975, topical chemotherapy at this Institute has involved the alternate application of mafenide acetate and silver sulfadiazine at 12-hour intervals to the wounds of patients whose burns have exceeded 30% TBS. Mafenide acetate is applied during the daylight hours and silver sulfadiazine at night to minimize post-application discomfort at bedtime and allow the patient to sleep undisturbed. In addition, this combination therapy minimizes the exacerbation of post-traumatic tachypnea by mafenide acetate and increases the antimicrobial spectrum of topical chemotherapy.

Once a diagnosis of bacterial burn wound invasion is confirmed, topical therapy is changed to mafenide acetate alone; appropriate systemic antibiotics are instituted, usually an aminoglycosidic antibiotic plus a semisynthetic penicillin for control of Gram-negative bacteria and an antibiotic effective against Gram-positive bacteria. In addition, subeschar clysis with a semisynthetic penicillin is instituted and repeated every 12 hours in areas of documented bacterial burn wound invasion (3). Following the institution of systemic and local antibiotic therapy a decision is made whether to excise invaded tissue. Excision to the level of the investing fascia is the operation of choice unless infection in an extremity has progressed subfascially, then amputation to ablate subfascial infection should be considered (1). If the infection extends subfascially on the torso, local debridement of infected subfascial tissue is carried out.

If mycotic burn wound invasion is identified and the patient has systemic evidence of infection, excision of involved tissue is carried out as described above and appropriate systemic antifungal agents are employed to control systemic dissemination.

Invasive burn wound sepsis caused by *Pseudomonas aeruginosa* was the form of this disease originally described (7). Despite the paucity of evidence for in vitro resistance to mafenide acetate of the *Pseudomonas* organisms recovered from our burn patients, *Pseudomonas* was recovered from the topically treated burn wounds in 55 of 97 patients (57%) with histologic evidence of burn wound invasion and from 39 of 57 (68%) patients dying from burn wound infection. Only *Pseudomonas* was present on cultures of wound biopsy material in 44 of the 55 patients with burn wound invasion, while an additional 11 patients had *Pseudomonas* present in combination with one or more other organisms. The organisms recovered by burn wound biopsy in 97 patients (Table III) indicate that *Pseudomonas aeruginosa* remains as the predominant offender, but the causative organisms are myriad and reflect opportunistic infection of a compromised host by any of the microbial inhabitants of the burn wound. The recovery of the same organism from the blood and the wound in 92% (69 of 75 patients) speaks for the invasiveness of bacterial burn wound infection. The relatively infrequent recovery of organisms from the blood in patients with fungal burn wound invasion (5 of 22) suggests either low virulence or the well-known limitations of mycologic culture technics. Decreased wound perfusion as evidenced by peripheral vasoconstriction, decreased urine output, decreased blood pressure, and the use of pressor agents in 31 patients with a life-threatening complication existing before documentation of burn wound invasion strongly suggests that the wound invasion in those patients was a terminal event and not the primary cause of demise.

That only 26% of deaths in this review were caused by BWS (57 of 218) is evidence of continued effectiveness of topical burn wound chemotherapy since BWS was the cause of death in 60% of fatally burned patients in the pre-topical chemotherapeutic era (6). The mortality of 77 patients with generalized burn wound infection was 96% (three survivors). The mortality among 20 patients with focal burn wound invasion was 70% (six survivors), as reflected in Table II. The average age of 21 years of the nine surviving patients was lower than the average ag of patients that died (Table I) and six of nine surviving patients had focal disease.

These 97 patients with burn wound infection demonstrate that although *Pseudomonas* is the most frequent offending organism, a variety of microorganisms cause infections in the severely burned, compromised host. In two thirds of patients with histologically documented BWI, that disease was considered to be the principal cause of death; however, in the other one third of p. ients it was not the principal cause of death but was co o have occurred preterminally with other complicatio sponsible for death. Survival from focal burn wound infectio more likely than survival following generalized burn wound infection. The treatment of established burn wound invasion must be based on the status of the individual patient and his burn wound. The various treatment regimens employed for these patients resulted in a 9% survival in this series.

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DISCUSSION

DR. C. EDWARD HARTFORD (Crozer-Chester Medical Center, Upland, Chester, PA 19013): I would like to thank Doctor McManus for the opportunity of viewing the paper ahead of time.

In a series of papers in 1964–1965 Teplitz and Moncrief and others at the Institute of Surgical Research defined burn wound sepsis, a prime criterion of which was the histologic confirmation of bacterial invasion of viable tissue. In 1975 Pruitt and Foley, from the same Institute, reviewed the use of biopsy to evaluate the burn wound as a source of infection among patients with clinical sepsis, advocated a system of grading which differentiated simple microbial colonization of the eschar from invasive burn wound infection, emphasized that the only reliable way to confirm invasive infection is by histologic means, and found an exceptionally high mortality with bacterial invasion of viable tissue.

In that background the authors have reviewed the recent burn wound infection experience at the Institute. They point out that invasive infection of the burn wound is still with us, it is associated with a substantial incidence of clinical systemic sepsis and a substantial incidence of death, that *Pseudomonas* at least in their experience remains a serious pathogen, and that the cornerstone of diagnosis is histologic proof of invasion of viable tissue.

Doctor McManus and coauthors also point out that not all patients die entirely from burn wound invasion. They also indicate that limited or focal burn wound invasive infection (and by that they define 'limited' or 'focal' as less than the area of one extremity) without a positive blood culture has a more favorable anecdotal prognosis than does generalized burn wound invasive infection with positive blood cultures.

In any biological system some will survive, no matter how serious the illness. Therefore in this series, based on the few surviving patients, I do not believe the authors have shed light on the treatment of invasive burn wound infection. The efficacy of subeschar instillation of antibiotics has never been substantiated, and it has yet to be proved that excisional therapy in the throes of sepsis is advantageous. I am making this a point of discussion because this was brought out in the abstract.

I would like to ask Doctor McManus if, based on the review of this information, he has an opinion about the efficacy of subeschar instillation of antibiotics in excisional therapy, and whether as a result of this review the authors have any recommendations for alteration of therapy.

DR. JOHN F. BURKE (Massachusetts General Hospital, Boston 02114): I would like to ask Doctor McManus if he would tell us a little bit more about the topical therapy that goes along with fungal infection. Is there any relationship between development of fungal infection in your experience and types of topical therapy?

DR. WILLIAM F. MCMANUS (Closing): I would like to thank the discussants for their comments and questions. Many of the answers will appear in the final text, however, time constraints have precluded detailed presentation today.

In answer to Doctor Burke's question, during the period of this study we have applied mafenide acetate and silver sulfadiazine alternately, at 12-hour intervals, to the wounds of patients whose burns exceeded 30% of the total body surface. We apply the mafenide acetate during the daylight hours and the silver sulfadiazine at night to minimize post-application discomfort and allow the patient to sleep. This combination therapy minimizes the exacerbation of post-traumatic tachypnea by mafenide acetate and increases the antimicrobial spectrum of the topical therapy.

I have no data to support any relationship between topical chemotherapy and the subsequent development of mycotic burn wound infection.

In answer to Doctor Hartford's questions, the purpose of this review was to identify the current spectrum of microbial organisms responsible for burn wound infection; to document the incidence of burn wound invasion as a primary cause of mortality or as a periterminal event when other disease was responsible for mortality; to describe the current burn wound management at this Institute; and to report the results of the current treatment of burn wound infection.

[Slide] In this group of 97 patients, the treatment of burn wound invasion has resulted in nine survivors. Once burn wound invasion is histologically documented, the topical agent is changed to mafenide acetate alone since no in vitro resistance to *Pseudomonas* has been identified to date. Appropriate systemic antimicrobial treatment is also instituted. In addition the subeschar administration of a semisynthetic penicillin such as carbenicillin and excision of infected tissue is performed as indicated by the nature and extent of burn wound infection. Burn wound invasion cannot be cured unless sepsis is controlled and the wound promptly and definitively closed.